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10/577,614	04/20/2007	Simon Feldbaek Nielsen	65487(50533)	5411

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EXAMINER	
CUTLIFF, YATE KAI RENE	
ART UNIT	PAPER NUMBER
1621	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/577,614	NIELSEN, SIMON FELDBAEK	
	Examiner	Art Unit	
	YATE' K. CUTLIFF	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39 – 44, 46 - 49, 55 - 61* is/are pending in the application.

4a) Of the above claim(s) *41,59 and 60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39 – 40, 42 - 44, 46 - 49, 55 – 58 and 61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 39 – 44, 46 - 49, 55 - 61 are pending.

Claims 1 - 38, 45 and 50-54 have been canceled

Claims 39 – 40, 42 - 44, 46 - 49, 55 – 58 and 61 are rejected.

Claims 41, 59 and 60 are withdrawn.

2. Newly submitted claim 59 and 61are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claims 59 and 61 are drawn the species for Y1 and Y2 defined as substituents (A) and (B), which were not elected by applicant in Applicant's Response to the dated June 16, 2008.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 59 and 61 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Information Disclosure Statement

3. The information disclosure statement filed October 13, 2006 fails to comply with 37 CFR 1.97, 1.98 and MPEP § 609 because the list of published foreign applications fail to provide the publication date of the application. Additonally, the publications listed do nit identify the title of the document. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this

information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Response to Amendment

4. The amendment to claims 39, 56, 58, and new claims 59 - 61, submitted March 2, 2009 is acknowledged and entered.

Response to Arguments

5. Applicant's arguments, see pages 10 and 11, filed March 2, 2009, with respect to the rejection(s) of claim(s) 39-40, 42-49 and 55-58 under 102(b) have been fully considered and are persuasive in view of the amendment. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Shinma's (US 4,327,088) as set out below.

Specification

6. The disclosure is objected to because of the following informalities: to because on page 35 at line 11, the identification of the bactericidal compound of Figure 2 is different from the identifying information on Figure 2.

Appropriate correction is required.

7. The disclosure is objected to because of the following informalities: to because on page 36 at line 22, the identification number for E.coli is incorrect.

Appropriate correction is required.

Claim Objections

8. Claim 56 is objected to under 37 CFR 1.75 as being in improper form because the claim depends on canceled claim 52. See MPEP § 608.01(n). Accordingly, the claim 56 not been further treated on the merits.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 58 and 61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being the elected species (i.e. D-001) may be enabling for inhibiting the growth of *Staphylococcus aureus ATCC29213; Staphylococcus aureus ATCC33591; Staphylococcus intermedius #2357(clinical isolate from the Copenhagen area); Enterococcus faecalis ATCC29212;Enterococcus faecium #17501 (vancomycin-resistant clinical isolate); Streptococcus pneumoniae #998 (clinical isolate); Streptococcus pyogenes #14813 (clinical isolate); Streptococcus agalactiae #19855 (clinical isolate); Eschericia coi ATCC25922 and Eschericia coil ESS*, does not reasonably provide enablement for treating any and all bacterial infections. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

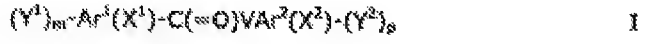
The test for enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information

known in the art without undue experimentation (United States v. Telectronice, 8, USPQ2D 1217 (Fed. Cir, 1988). Whether undue experimentation is needed is not based upon a single factor but rather in a conclusion reached by weighing many factors. The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims: **(Elected species only)**

The claims are drawn to a method for treating bacterial infections in a mammal. The instant method uses the compound of formula (I);



The variable V represents, -CH2-CH2-, -CH=CH-, CH≡CH-, and the remaining variables are set out in claim 58.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. Haraguchi et al. (Phytochemistry, 1998) discloses a similar compound that has anti-bacterial activity against some gram positive bacteria. (see abstract & page 126).

Further, according to Holland et al. between 1960 and 1974, 826 specimens yielded 689 positive cultures , of which 403 contained anaerobic bacteria. (Journal of Clinical Microbiology, 1997). Furthermore, from the encyclopedia farlex it is stated that only a few thousand species of bacteria have been grown in laboratory cultures.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each

embodiment to be individually assessed for physiological activity. *In re Fisher,* 427 F.2d 833,166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Applicant's are claiming an intent method of use, by using the compounds of formula (I) as effective against all forms of bacteria. As such the specification fails to enable the skilled artisan to use the compounds of formula (I) for treating bacterial infections other than those associated with: of *Staphylococcus aureus ATCC29213; Staphylococcus aureus ATCC33591; Staphylococcus intermedius #2357(clinical isolate from the Copenhagen area); Enterococcus faecalis ATCC29212;Enterococcus faecium #17501 (vancomycin-resistant clinical isolate); Streptococcus pneumoniae #998 (clinical isolate); Streptococcus pyogenes #14813 (clinical isolate); Streptococcus agalactiae #19855 (clinical isolate); Eschericia coi ATCC25922 and Eschericia coil ESS*. In addition, there is not proof that the claimed compounds of formula (I) inhibit the bacterial growth of all forms of bacteria in mammals. Furthermore, there is no established correlation between the MCI and MBC activity presented in the specification and the treatment of all aerobic and anaerobic forms of bacteria other than those disclosed. Those skilled in the art would not accept allegations in the instant specification to be reliable predictors of success in all instances.

Hence, one of skill in the art is unable to fully predict possible results from the administration of the instant compounds of the claims due to the unpredictability of the treatment of the various types of bacterial because of their varied characteristics, i.e. shape, DNA sequence, metabolic activities, biochemical reactions and antigenic

properties. Because of these factors one of ordinary skill in the art would not readily accept on its face the compound of formula (I) as a treatment regiment for all forms of bacteria.

(5) The relative skill of those in the art:

The relative level of skill possessed by one of ordinary skill in the art of medical research is relatively high, as a majority of lead investigators directing scientific research and development in this particular technology area posses a Ph.D. in a scientific discipline such as organic synthetic chemistry, biochemistry, medicinal chemistry, pharmacology, biology or the like.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for the inhibition of *Staphylococcus aureus ATCC29213; Staphylococcus aureus ATCC33591; Staphylococcus intermedius #2357(clinical isolate from the Copenhagen area); Enterococcus faecalis ATCC29212;Enterococcus faecium #17501 (vancomycin-resistant clinical isolate); Streptococcus pneumoniae #998 (clinical isolate); Streptococcus pyogenes #14813 (clinical isolate); Streptococcus agalactiae #19855 (clinical isolate); Eschericia coi ATCC25922 and Eschericia coil ESS*.

However, the specification does not provide any in vivo working examples for the vast species of bacteria that have been isolated or grown in laboratory settings.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to inhibiting the vast number of bacteria known and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 39 and 58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claims 39 and 58 identify the compound as the “general" formula (I). The term “general” leads to confusion over the intended scope of the claims. Applicant should remove this term.

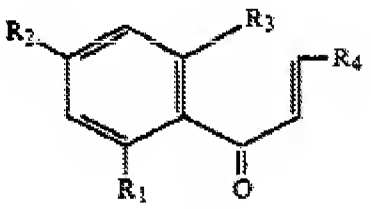
Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 39-40, 42 - 44, 46-49 and 55-57 rejected under 35 U.S.C. 102(b) as being anticipated by Shinma et al. 9US 4,327,088 and Kunitake (J. Am. Chem. Soc. 1981, vol. 103).

16. Shinma et al. discloses the following formula:



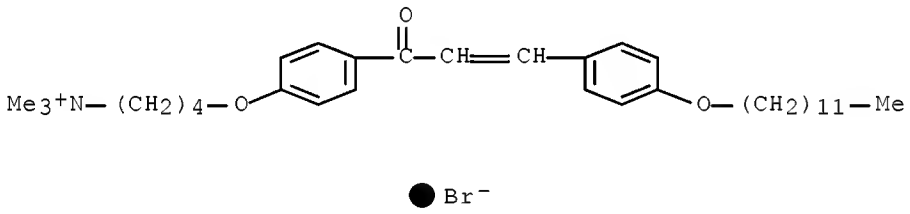
I

The above compound can be

2'-hydroxy-4',6'-dimethoxy-4-(methoxymethoxy)chalcone;

The above compound anticipates Applicant's claimed formula (I) when Shinma's R1 is hydroxy, R4 is phenyl with a substituted C1 alkoxy, and R2 and R3 are lower alkoxy. (see column 3, lines 15-25 & column 4 lines 30-31)

17. Kunitake et al. discloses the following compound.



The above compound anticipates Applicant's claimed formula (I). (see page 5405, #58 & page 5402, column 1 "Chemical Structures of Amphiphhiles", lines 5-8).

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

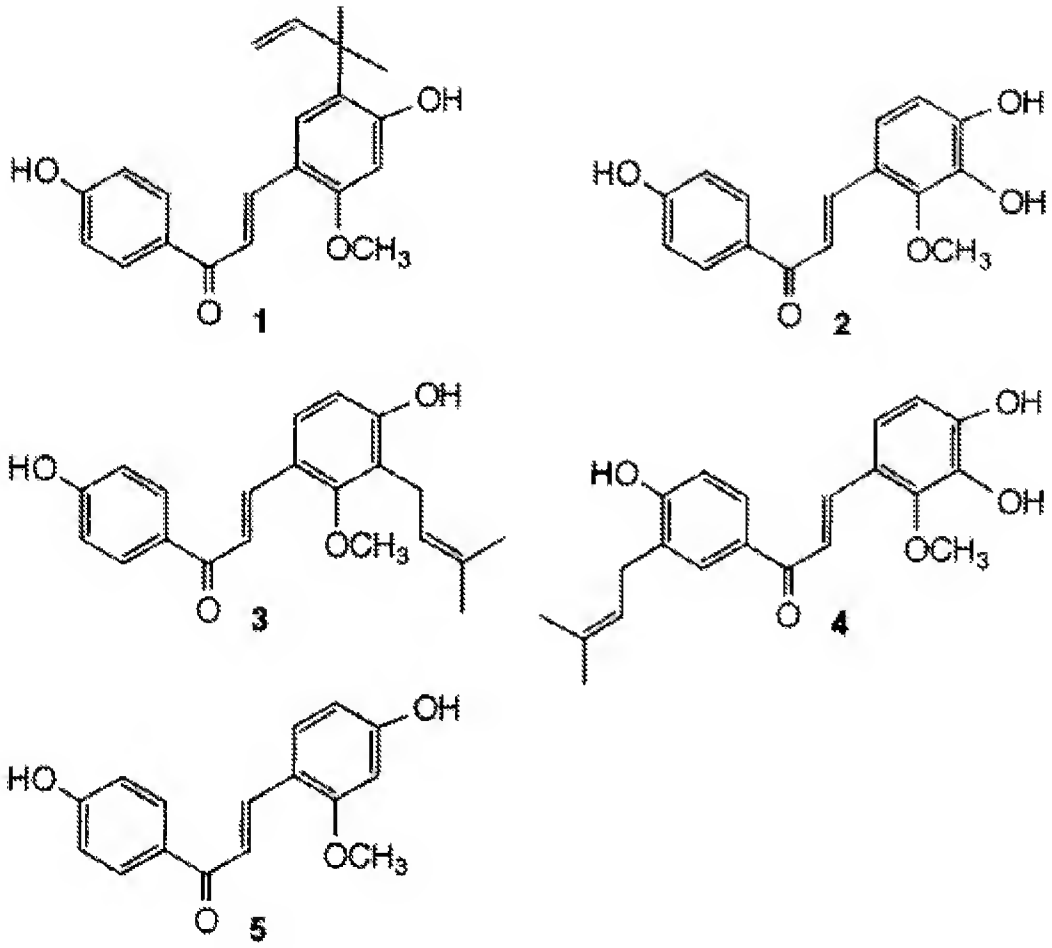
19. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

20. Claims 58 and 61 rejected under 35 U.S.C. 103(a) as being unpatentable over Haraguchi et al. (Phytochemistry, 1998), in view of Berge et al. (Journal of pharmaceutical Science, vol. 66, no. 1).

21. Rejected claims 58 – 61 are drawn to the compound of formula (I) where V is -CH2-CH2-, -CH=CH-, or CH≡CH-.

22. Haraguchi et al. discloses the following compounds that demonstrate antibacterial action.



Also, in Table 1 is a listing of the microorganisms affected by the antimicrobial activity of compounds of Haraguchi et al.

The difference between Haraguchi et al. and Applicant's claimed invention is that Haraguchi et al. does not disclose the salt version of the compounds and it does not disclose an amine form.

23. However, with regard to the salt from Berge et al. discloses known pharmaceutical salt anions. (see page 5 Table I). Further, it is stated that The chemical, biological, and economic characteristic of medicinal agents can be manipulated and hence, often optimized by conversion to a salt form.

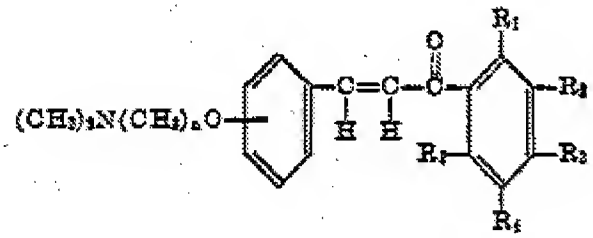
In light of the antimicrobial activity obtained by Haraguchi et al., it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to include make the salt from of the compounds of Haraguchi et al. by using any one of the available anions disclosed by Berge et al. "[A]n implicit motivation to combine exists not only when a suggestion may be gleaned from the prior art as a whole, but when the improvement' is technology-independent and the combination of references results in a product or process that is more desirable, for example because it is stronger, cheaper, cleaner, faster, lighter, smaller, more durable, or more efficient. Because the desire to enhance commercial opportunities by improving a product or process is universal-and even common-sensical we have held that there exists in these situations a motivation to combine prior art references even absent any hint of suggestion in the references themselves. In such situations, the proper question is whether the ordinary artisan possesses knowledge and skills rendering him capable of combining the prior art references." (DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co., 464 F.3d 1356, 1368, 80 USPQ2d 1641, 1651 (Fed. Cir. 2006)).

Therefore, in view of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common senses.

24. Claim 39-40, 42 - 44, 46-48, 58 and 61 rejected under 35 U.S.C. 103(a) as being unpatentable over Packman et al. (US 3,407,233

25. Rejected claims 39-40, 42-44, 46-48 are to compound of formula (I) where V is -CH=CH-.

26. Packman et al. discloses the following formula:



in which n is 2 or 3, R_1, R_2, R_3, R_4 and R_5 are hydrogen or methoxy, at least two of R_1, R_2, R_3, R_4 and R_5 being methoxy.

The difference between Applicant's claimed compound and Packman et al. is that it does not disclose Q anion.

27. However, Packman states that if the acid salts are desired they are produced by reacting the resulting chalcone with the appropriate acid under anhydrous conditions.

The prior art of Packman. discloses compounds of their formula which encompass Applicant's claimed compounds. The difference between Packman et al. and the claimed inventions is that it does not teach the invention with particularity so as to amount to anticipation (See M.P.E.P. § 2131: "[t]he identical invention must be shown in as complete detail as is contained in the ... claim." Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an ipsissimis verbis test, i.e., identity of

terminology is not required. In re Bond, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

However, based on the above, Packman teaches the elements of the claimed invention with sufficient guidance, particularity, and with a reasonable expectation of success, that the invention would be prima facie obvious to one of ordinary skill (the prior art reference teaches or suggests all the claim limitations with a reasonable expectation of success. See M.P.E.P. § 2143).

Allowable Subject Matter

28. The elected species: (2-{3-[3-(2-Chloro-4-methoxy-phenyl)-3-oxo-propenyl]-3',5'-dimethyl-biphenyl-4-yloxy}-ethyl)-trimethyl-amonium, iodide, has been searched and is deemed free of the prior art. As stated in the Office Action mailed October 2, 2008, the search was therefore expanded as called for under current Office Markush examination practice, a compound-by-compound search, to include a single additional compound; where V is -CH2-CH2-, -CH=CH-, CH≡CH-, Ar1 and Ar2 are aryl (substituted or unsubstituted), Y1 and Y2 are independently-O-Z-N+(R1)(R2) Q-; and were p, m, Z, R1, R2, R4, Q and X1 and X2 are as defined in the claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to YATE' K. CUTLIFF whose telephone number is (571)272-9067. The examiner can normally be reached on M-TH 8:30 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Daniel M. Sullivan can be reached on (571) 272 - 0779. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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